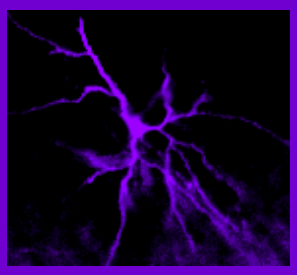

Northwestern University Institute for Neuroscience

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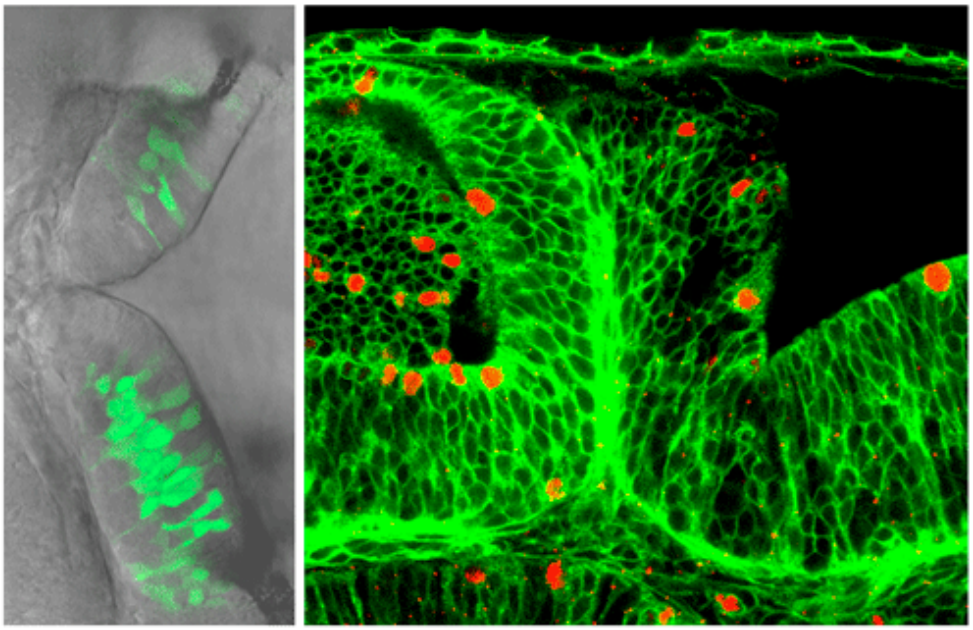
Research Interest

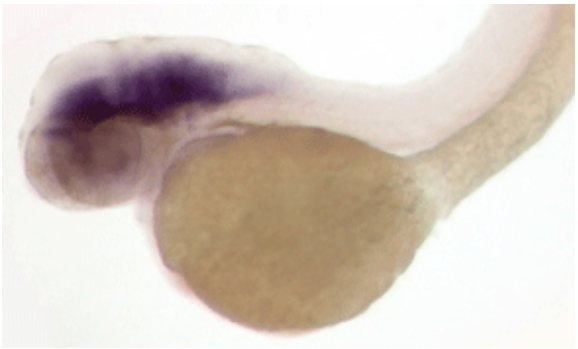
Embryo development required both proper specification of several cell types and concurrently their organization in complex structures. We have chosen the zebrafish as especially suitable animal model for both patterning and morphogenetic studies. The zebrafish embryo is transparent and direct observation of the cellular behavior and tissue organization is possible. Existing transgenic lines, which express reporter GFP in a tissue specific manner greatly, enhance our ability to follow individual cells. We have developed techniques that allow us to observe a live embryo under the confocal microscope and study cells appearance and their migration with height resolution.



Left panel: Localization of Purkinje cell precursors in forming zebrafish cerebellum in a live embryo; overlapped DIC picture and single confocal section. Right panel: confocal

microscopy section of medial part of forming cerebellum;(transgenic line generated in B. Appel laboratory Shin, J. et al 2003) cell shapes visualized by membrane localized GFP, red staining indicate mitotically active cells.

The cellular interactions and the role of each cell type in the assembly of such a complex structure like the cerebellum is for us a particularly interesting subject. Those studies are directed by Dr. Jolanta Topczewska, Research Assistant Professor, CMIER. The cerebellum is one of the earliest structures formed in the brain but its development continues long after birth. Such long developmental schedule makes it vulnerable to developmental defects and as a result, numerous clinical syndromes are known with cerebellar involvement. The Purkinje neuron precursor cells are one of the earliest cells that leave the ventricular zone and form a foundation for the next developmental steps of the cerebellum formation. The combination of zebrafish transgenic techniques with classical genetic gives us unique possibility to study the migratory behavior and proliferation of Purkinje precursors during early steps of development. Recently we had identified the zebrafish genetic deficiency that alters in homozygote embryos behavior of the Purkinje precursors cells. Purkinje cells in mutant are more numerous, mitotically active and have abnormal morphologies. Initial characterization of the genetic deficiency determined at least 15 novel genes located in this deletion. Preliminary analysis of identified genes suggests that several of them might be involved in a cell cycle control or cell-cell adhesion. Those studies provide us with unique possibility to identify new genes that are involved in early steps of cerebellum formation control.



Expression pattern of zebrafish glypican 1 homologue at the second day of development.

We are also interested in function of proteins from Glypican family, the extracellular heparan sulfate proteoglycans. Our work and others established that during development Glypicans interact with several important signaling molecules including FGF, BMP, Hedgehog and WNT family members. We have shown that the Glypican 4/6 Knypek function as a part of WNT signaling pathway controlling the cells movement during gastrulation. We are currently studying role of Glypican Knypek in morphogenesis of neural crest derived head cartilage. Additionally, we have isolated zebrafish homologues of a glpican 1. Those genes similar to other vertebrates are strongly expressed in central nervous system including the cerebellum. We are studying developmental role of newly isolated glypican genes with special emphasis on their function in cerebellum development. We are also interested in characterization signaling pathways in which Glypican 1 participate.

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